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FILE COVERS 1907 - 3 Feb 2003 VOL 138 ISS 6
 FILE LAST UPDATED: 2 Feb 2003 (20030202/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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(FILE 'HOME' ENTERED AT 15:07:22 ON 03 FEB 2003)

FILE 'REGISTRY' ENTERED AT 15:07:34 ON 03 FEB 2003

E MS-HBP1/CN
 E MS-HBP1
 E MSHBP1/CN
 E MSHBP1
 L1 2 S MS(W) (HBP1 OR HBP(W)1)
 E FS-HBP1/CN
 L2 2 S FS(W) (HBP1 OR HBP(W)1)
 E FS-HBP2/CN
 E FS-HBP2
 L3 2 S FS(W) (HBP2 OR HBP(W)2)
 E I-RET 6/CN
 E D-RET 6/CN
 E D-RET 6/CN
 L4 1 S E4
 L5 2 S D(W) (RET6 OR RET(W)6)
 E HISTACALIN/CN
 E HISTACALIN/CN
 L6 1 S E2
 E HISTACALIN PROTEIN/CN

FILE 'HCAPLUS' ENTERED AT 15:30:21 ON 03 FEB 2003

L7 5 S L1 OF MS(W) (HBP1 OR HBP(W)1)
 L8 5 S L2 OF FS(W) (HBP1 OR HBP(W)1)
 L9 5 S L3 OF FS(W) (HBP2 OR HBP(W)2)
 L10 289 S L4 OF L5 OR D(W) (RET6 OR RET(W)6)
 L11 315 S L6 OF HISTACALIN?
 L12 6 S L7 OR L8 OR L9 OR L10 AND (?CONJUNCT OR EYE? OR OCUL?)

FILE 'HCAPLUS' ENTERED AT 15:39:10 ON 03 FEB 2003

Searched by M. Smith

=> d ibib abs hitrn 112 1-6

L12 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:168020 HCAPLUS
 DOCUMENT NUMBER: 134:217189
 TITLE: Treatment of allergic rhinitis with proteins from ticks
 INVENTOR(S): Nuttall, Patricia Anne; Paesen, Guido Christiaan
 PATENT ASSIGNEE(S): Evolutec Limited, UK
 SOURCE: PCT Int. Appl., 19 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2001016164 | A2 | 20010308 | WO 2000-GB3287 | 20000824 |
| WO 2001016164 | A3 | 20010503 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OL, OM, OS, PA, PE, PG, PH, PK, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, FG, KZ, MD, RU, TJ, TM | | | | |
| FW: GH, GM, KE, LS, MW, ME, SE, SL, SS, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GE, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MF, NE, SN, TD, TG | | | | |
| BR 2000013655 | A | 20020507 | BR 2000-13655 | 20000824 |
| EP 1207399 | A2 | 20020529 | EP 2000-954788 | 20000824 |
| F: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| US 2002193306 | A1 | 20021219 | US 2002-87195 | 20020301 |
| PRIORITY APPL. INFO.: GB 1999-20673 A 19990901 | | | | |
| WO 2000-GB3287 W 20000824 | | | | |

AB The invention relates to the discovery that various proteins isolated from ticks are effective in the treatment and prevention of allergic rhinitis. These proteins may most suitably be applied to an affected area and are thus effective to treat this condition and to ameliorate its symptoms. Human subjects were challenged with histamine and then were treated with histamine-binding protein, **MS-HBP1**.

L12 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:167826 HCAPLUS
 DOCUMENT NUMBER: 134:217188
 TITLE: use of histacalin protein for treatment or prevention of conjunctivitis
 INVENTOR(S): Nuttall, Patricia Anne; Paesen, Guido Christiaan
 PATENT ASSIGNEE(S): Evolutec Limited, UK
 SOURCE: PCT Int. Appl., 19 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

WD 2001015719 A2 20010308 WD 2000-GB3282 20000824
 WD 2001015719 A3 20010510
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CR, CU, CZ, DE, DK, DM, EE, ES, FI, FR, GD, GE, GH, GM, HR,
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LF, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG, SI, SK, SL, TJ, TM, TP, TT, TZ, UA, UG, US, UZ, VN,
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TC, TM
 PW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TG, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MF, NE, SH, TD, TG

BF 2000013665 A 20020514 BR 2000-13665 20000824
 EF 2007898 A2 20020529 EP 2000-954784 20000824
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL

US 2002151499 A1 20021017 US 2002-85572 20020227
 PRIORITY APPLN. INFO.: GB 1994-20674 A 19990901
 WO 2000-GB3282 W 20000824

AB Various histacalin proteins isolated from ticks are effective in the treatment of conjunctivitis. These proteins may most suitably be applied topically to an affected area and are effective to ameliorate the symptoms of this condition.

L12 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:374997 HCAPLUS
 DOCUMENT NUMBER: 131:154999
 TITLE: Tick histamine-binding proteins: isolation, cloning, and three-dimensional structure
 AUTHOR(S): Paesen, G. C.; Adams, P. L.; Harlos, K.; Nuttall, P. A.; Stuart, D. I.
 CORPORATE SOURCE: Institute of Virology and Environmental Microbiology, Natural Environment Research Council, Oxford, OX1 3SR, UK
 SOURCE: Molecular Cell (1999), 3(5), 661-671
 CODEN: MOCEFL; ISSN: 1097-2765
 PUBLISHER: Cell Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB High-affinity histamine-binding proteins (HBPs) were discovered in the saliva of Rhipicephalus appendiculatus ticks. Their ability to outcompete histamine receptors indicates that they suppress inflammation during blood feeding. The crystal structure of a histamine-bound HBP, detd. at 1.25 Å. resoln., reveals a lipocalin fold novel in cntg. two binding sites for the same ligand. The sites are orthogonally arranged and highly rigid and form an internal surface of unusual polar character that complements the physicochem. properties of histamine. As sol. receptors of histamine, HBPs offer a new strategy for controlling histamine-based diseases.

IT 200220-32-2 200220-33-3 200220-34-4

RL: PFP (Properties)
 (amino acid sequence; isolation, cloning, mol. characterization and three-dimensional structure of sex-specific tick histamine-binding proteins)

IT 200220-28-6, GenBank U96080 200220-29-7, GenBank U96081
 200220-30-0, GenBank U96082

RL: PFP (Properties)
 (nucleotide sequence; isolation, cloning, mol. characterization and three-dimensional structure of sex-specific tick histamine-binding proteins)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:359659 HCAPLUS

DOCUMENT NUMBER: 131:28315

TITLE: Cloning and functions of vasoactive amine-binding proteins from ticks

INVENTOR(S): Nuttall, Patricia Ann; Paesen, Guido Christian.

PATENT ASSIGNEE(S): Oxford Vacs Ltd., UK

SOURCE: ECT Int. Appl., 84 pp.

CODEN: PXXXX2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9927104 | A1 | 19990603 | WO 1998-GR3530 | 19981126 |
| W: AU, AM, AT, AU, AZ, BA, BB, BG, BP, BY, CA, CH, CN, CU, CE, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, VN, YU, ZW, AM, AS, BY, KG, KZ, MD, RU, TJ, TM, RW, GR, BM, HE, LS, MW, SO, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GE, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, ME, NE, SN, TD, TG | | | | |
| CA 2309809 | AA | 19990603 | CA 1998-2309809 | 19981126 |
| AU 9911511 | A1 | 19990615 | AU 1999-12511 | 19981126 |
| EP 1034273 | A1 | 20000913 | EP 1998-955786 | 19981126 |
| E: AT, BE, CH, DE, DK, ES, FR, GB, GE, IE, LI, LU, NL, SE, MC, PT, IE, FI, RO | | | | |
| BR 9815056 | A | 20001003 | BR 1998-15056 | 19981126 |
| JP 1002508927 | T2 | 20020316 | JP 2000-522246 | 19981126 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | GB 1997-25046 | A 19971126 |
| | | | GB 1998-13917 | A 19980626 |
| | | | WO 1998-GB3530 | W 19981126 |

AB The present invention relates to histamine and serotonin binding mols. that possess a binding site with the precise mol. configuration that is necessary to confer on the mol. a high affinity for histamine. The invention includes proteins, peptides and chem. compds. that possess this mol. configuration and that are thus able to bind to histamine with high affinity. These mols. may be used in the regulation of the action of histamine or serotonin, the detection and quantification of histamine or serotonin and in the treatment of various diseases and allergies. The mols. may also be used as components of vaccines directed against blood-sucking ectoparasites. Vasoactive amine binding proteins (VABPs) are provided that specifically bind to vasoactive amines with a dissocn. const. of 10^{-7} M and which belong to the same protein family as

MS-HBP1, FS-HBP1, FS-

HBP2 and D.RET6. Thus, 11 VASPs were isolated, and their cDNAs cloned and sequenced, from ticks: **FS-HBP1**

(female-specific histamine-binding protein 1), **FS-HBP2**

(female-specific histamine-binding protein 2), **MS-HBP1**

(male-specific histamine-binding protein 1), and Ra-Res from Rhipicephalus appendiculatus; D.RET6 from Dermacenter reticularis; Av-HBP from Amblyomma variegatum; and 5 related Ih/Bm-HBP proteins from a mixed Ixodes hexagonus/Boophilus microplus cDNA expression library. These VASPs possess similar amino acid sequences and predicted secondary structures.

The VASPs bind histamine in mammals, and can be used as anti-inflammatory agents to regulate histamine action and to control its pathol. effects. The crystal structure of **FS-HBP2** to 2.24 Å. resoln. was used to design a synthetic cyclic octapeptide (-Ala-Glu-Ala-Phe-Ala-Glu-Ala-Trp-) with histamine binding activity.

IT 200220-32-2 200220-33-3 200220-34-4

PL: BAC (Biological activity or effector, except adverse); BPP (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (amino acid sequence; cloning and functions of vasoactive amine-binding proteins from ticks)

IT 200220-28-6P 200220-29-7P 200220-30-0P

PL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PPEP (Preparation); USES (Uses) (nucleotide sequence; cloning and functions of vasoactive amine-binding proteins from ticks)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE FE FORMAT

L12 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:270816 HCAPLUS

DOCUMENT NUMBER: 131:53579

TITLE: Inhibitory effects of tetrandrine and related synthetic compounds on angiogenesis in streptozotocin-diabetic rodents

AUTHOR(S): Kobayashi, Shinjiro; Kimura, Ikuko; Fukuta, Mizuki; Kentani, Hitoshi; Inaba, Kazuhiko; Niwa, Masashi; Mita, Shiro; Kimura, Masayasu

CORPORATE SOURCE: Department of Pharmacology, Faculty of Pharmaceutical Sciences, Hokuriku University, Kanazawa, 920-1181, Japan

SOURCE: Biological & Pharmaceutical Bulletin (1999), 22(4), 360-365

CODEN: BPBLEO; ISSN: 0918-6158

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Structure-activity relationships of tetrandrine, isolated from a Kampo medicine, *Stephania tetrandrae* S. Moore (root), and related synthetic compds., were investigated in in vitro fetal bovine serum (FBS)-stimulated angiogenesis of cultured choroids in streptozotocin-diabetic Wistar rats, and air-pouch granuloma angiogenesis in vivo in diabetic mice. Tetrandrine, KS-1-1 (6,7-dimethoxy-1-[[4-[5-(6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquino linyl)methyl-2-methoxy]phenoxy]benzyl]-2-methyl-1,2,3,4-tetrahydroisoquino line), and KS-1-4 (6,7-dimethoxy-1-[[4-[4-(6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquino linyl)methyl]phenoxy]benzyl]-2-methyl-1,2,3,4-tetrahydroisoquinoline), potently inhibited choroidal angiogenesis and air-pouch granuloma angiogenesis in the diabetic state. Their inhibitory effects on diabetic choroids were greater than those on normal choroids. Among these compds., KS-1-4 inhibited only diabetic angiogenesis. These compds. significantly inhibited FBS-stimulated tube formation in vascular endothelial cells from normal rats. Tetrandrine and KS-1-4, but not KS-1-1, inhibited vascular endothelial growth factor- and platelet-derived growth factor-BB-stimulated angiogenesis in normal choroids. The bis[tetrahydroisoquinoline] moiety, connected by oxy-bis[phenylenemethylene] and 2,2'-dimethyl groups in tetrandrine, contributes to the inhibition of diabetic choroidal angiogenesis. KS-1-4 may be a candidate for anti-chorioidopathy and retinopathy drugs in the diabetic state.

IT 485-19-8, (+)-Reticuline

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(inhibitory effects of tetrandrine and related synthetic compds. on arginogenesis in streptozotocin-diabetic rodents)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE FE FORMAT

L12 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:776255 HCAPLUS

DOCUMENT NUMBER: 128:57765

TITLE: Cloning and functions of vasoactive amine-binding proteins from ticks

INVENTOR(S): Paesen, Guido Christian; Nuttall, Patricia Ann.

PATENT ASSIGNEE(S): Oxford Vacs Ltd., UK; Paesen, Guido Christian; Nuttall, Patricia Ann

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9744451 | A2 | 19971127 | WO 1997-GB1372 | 19970519 |
| WO 9744452 | A3 | 19980219 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JF, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM | | | | |
| FW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2253924 | AA | 19971127 | CA 1997-2253924 | 19970519 |
| AU 9729071 | A1 | 19971209 | AU 1997-29071 | 19970519 |
| AU 725630 | B2 | 20001019 | | |
| EP 906425 | A2 | 19990407 | EP 1997-923104 | 19970519 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO | | | | |
| BR 9709101 | A | 19990303 | BR 1997-9101 | 19970519 |
| CN 1225683 | A | 19990211 | CN 1997-196317 | 19970519 |
| JP 2000512489 | T2 | 20000926 | JP 1997-541799 | 19970519 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | GB 1996-10484 | A 19960513 |
| | | | GB 1997-7844 | A 19970413 |
| | | | WO 1997-GB1372 | W 19970519 |

AB Vasoactive amine binding proteins (VABPs) are provided that specifically bind to vasoactive amines with a dissociation constant of $<10^{-7}$ M and which belong to the same protein family as **MS-HBP1**, **FS-HBP1**, **FS-HBP2** and **D.RET6**. Thus, 4 VASPs were isolated, and their cDNAs cloned and sequenced, from ticks: **FS-HBP1** (female-specific histamine-binding protein 1), **FS-HBP2** (female-specific histamine-binding protein 2), and **MS-HBP1** (male-specific histamine-binding protein 1) from *Rhipicephalus appendiculatus*; and **D.RET6** from *Dermacentor reticularis*. These 4 VASPs possess similar amino acid sequences and predicted secondary structures. The VASPs bind histamine in mammals, and can be used as anti-inflammatory agents to regulate histamine action and

to control its pathol. effects.

IT 200220-32-2 200220-33-3 200220-34-4

RL: BAC (Biological activity or effector, except adverse); BPP (Biological process); BSU (Biological study, unclassified); PPP (Properties); THU (Therapeutic use); BIOL (Biological study); PROCC (Process); USES (Uses) (amino acid sequence; cloning and functions of vasoactive amine-binding proteins from ticks)

IT 200220-28-6P 200220-29-7P 200220-30-0P

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PFEP (Preparation); USES (Uses) (nucleotide sequence; cloning and functions of vasoactive amine-binding proteins from ticks)

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L1 2 SEA FILE=PEGISTRY MS(W) (HBP1 OR HBP(W)1)
 L2 2 SEA FILE=PEGISTRY FS(W) (HBP1 OR HBP(W)1)
 L3 2 SEA FILE=PEGISTRY FS(W) (HBP2 OR HBP(W)2)
 L4 1 SEA FILE=PEGISTRY D-PETICULINE/CN
 L5 2 SEA FILE=PEGISTRY D(W) (RET6 OR RET(W)6)
 L6 1 SEA FILE=PEGISTRY HISTAC/CN
 L7 5 SEA FILE=HCAPLUS L1 OF MS(W) (HBP1 OR HBP(W)1)
 L8 5 SEA FILE=HCAPLUS L2 OF FS(W) (HBP1 OR HBP(W)1)
 L9 5 SEA FILE=HCAPLUS L3 OF FS(W) (HBP2 OR HBP(W)2)
 L10 283 SEA FILE=HCAPLUS L4 OF L5 OF D(W) (RET6 OR RET(W)6)
 L11 315 SEA FILE=HCAPLUS L6 OF HISTACALIN?
 L12 6 SEA FILE=HCAPLUS L7 OF L8 OF L9 OR L10 AND (?CONJUNCT OR EYE? OR OCUL?)
 L13 4 SEA FILE=HCAPLUS L11 AND (?CONJUNCT? OR EYE? OR ?OCUL?)
 L14 3 SEA FILE=HCAPLUS L13 NOT L11

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L14 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:795285 HCAPLUS

DOCUMENT NUMBER: 128:110395

TITLE: Compatibility of doxorubicin hydrochloride liposome injection with selected other drugs during simulated Y-site administration

AUTHOR(S): Trissel, Lawrence A.; Gilbert, Doward L.; Martinez, Juan F.

CORPORATE SOURCE: Division of Pharmacy, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: American Journal of Health-System Pharmacy (1997), 54(23), 2708-2713

CODEN: AHSPEK; ISSN: 1079-2082

PUBLISHER: American Society of Health-System Pharmacists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The compatibility of doxorubicin hydrochloride liposome injection with selected other drugs during simulated Y-site administration was studied. Five milliliters of doxorubicin hydrochloride liposome injection 0.4 mg/mL in 5% dextrose injection was combined with 5 mL of each of 82 other drugs in 5% dextrose injection or, if necessary to avoid incompatibilities with the diluent, 0.9% sodium chloride injection. The combinations were examd. with the unaided eye in fluorescent light and in high-intensity monodirectional light to enhance visualization of small particles and low-level turbidity. The turbidity of each combination was measured as

well. Particle sizing and counting were performed on selected combinations. Evaluations were performed initially and at one and four hours. All combinations were stored at room temp. (.apprx.23 .degree.C). Most of the test drugs were compatible with doxorubicin hydrochloride liposome injection during the four-hour observation period. However, practitioners should be cautious in administering any drug simultaneously with doxorubicin hydrochloride liposome injection until the integrity of the liposomes can be verified. Eighteen drugs exhibited unacceptable increases or decreases in measured turbidity or particulate formation within four hours. During simulated Y-site administration, doxorubicin hydrochloride 0.4 mg/mL (as the liposomal injection) in 5% dextrose injection was compatible with 64 of 82 other drugs for four hours at .apprx.23 .degree.C and was incompatible with 18 of the test drugs.

IT 66357-59-3, Ranitidine hydrochloride

PL: ADV (Adverse effect, including toxicity); BIOL (Biological study); (doxorubicin hydrochloride liposome injection compatibility with other drugs)

L14 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:678708 HCAPLUS

DOCUMENT NUMBER: 127:325983

TITLE: Compatibility of remifentanyl hydrochloride with

selected drugs during simulated Y-site administration

AUTHOR(S): Trissel, Lawrence A.; Gilbert, Doward L.; Martinez, Juan F.; Kim, Mia C.

CORPORATE SOURCE: Division of Pharmacy, Clinical Pharmaceuticals, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: American Journal of Health-System Pharmacy (1997), 54(19), 2192-2196

CODEN: AHSPEK; ISSN: 1079-2082

PUBLISHER: American Society of Health-System Pharmacists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The compatibility of remifentanyl hydrochloride with 90 other drugs during simulated Y-site administration was studied. Five milliliters of remifentanyl 25 and 250 .mu.g/mL (as hydrochloride) in 0.9% sodium chloride injection or 5% dextrose injection was combined with 5 mL of each of 90 other drugs in 5% dextrose injection or 0.9% sodium chloride injection. Each combination was prepd. in duplicate. The combinations were stored at .apprx.23 .degree.C under fluorescent light and examd. with the unaided eye and in high-intensity monodirectional light during the first 15 min after prepn. and at one and four hours. The turbidity of each combination was measured as well. Particle sizing and counting were performed for selected combinations. Most of the combinations exhibited no haze, turbidity, or color change throughout the study period. Remifentanyl 25 .mu.g/mL combined with chlorpromazine hydrochloride showed a small increase in haze within four hours. One of the combinations of remifentanyl 250 .mu.g/mL with cefoperazone sodium was un-acceptably hazy within one hour. The combination of remifentanyl 250 .mu.g/mL with amphotericin B formed a gross ppt. upon mixing. Remifentanyl 25 and 250 .mu.g/mL (as hydrochloride) in 0.9% sodium chloride injection was compatible for four hours at .apprx.23 .degree.C with all the drugs studied except chlorpromazine hydrochloride (with remifentanyl 25 .mu.g/mL), cefoperazone sodium (with remifentanyl 250 .mu.g/mL), and amphotericin B (with remifentanyl 250 .mu.g/mL in 5% dextrose injection).

IT 66357-59-3, Ranitidine hydrochloride

PL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(remifentanil hydrochloride compatibility with 90 pharmaceuticals)

L14 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:321916 HCAPLUS

DOCUMENT NUMBER: 125:18979

TITLE: Compatibility of thiotepa (lyophilized) with selected drugs during simulated Y-site administration

AUTHOR(S): Trissel, Lawrence A.; Martinez, Juan F.

CORPORATE SOURCE: M. D. Anderson Cancer Center, University of Texas, Houston, TX, 77030, USA

SOURCE: American Journal of Health-System Pharmacy (1996), 53(9), 1041-1045

CODEN: AHSPEK; ISSN: 1079-2082

PUBLISHER: American Society of Health-System Pharmacists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Five-milliliter samples of thiotepa (lyophilized) (1 mg/mL in 5% dextrose soln.) were combined with 5 mL each of 100 other drugs, including antineoplastics, anti-infectives, and supportive care drugs, in 5% dextrose or 0.9% NaCl. The combinations were stored at room temp. (.apprx.23.degree.) under const. fluorescent light. Visual examns. were performed with the unaided **eye** immediately and after 1 and 4 h and, if there was no obvious incompatibility, with a high-intensity monodirectional light beam to enhance visualization of small particles and low-level turbidity. The turbidity of each combination was measured as well. Particle sizing and counting were performed on selected solns. Two drugs exhibited incompatibilities with thiotepa. The thiotepa-cisplatin combination developed turbidity in 4 h, and the thiotepa-minocycline-HCl combination developed a bright yellow-green discoloration in 1 h. All the other test drugs were compatible with thiotepa for at .gtoreq.4 h at room temp.

IT **66357-59-3**, Ranitidine hydrochloride

RL: MSC (Miscellaneous); PEP (Physical, engineering or chemical process);

PRP (Properties); PROC (Process)

(physicochem. compatibility of drugs with thiotepa during simulated i.v. administration)

Show files

File 155:MEDLINE(R) 1966-2003/Jan W4
 (c)
 File 5:Biosis Previews(R) 1969-2003/Jan W4
 (c) 2003 BIOSIS
 File 34:SciSearch(R) Cited Ref Sci 1990-2003/Jan W4
 (c) 2003 Inst for Sci Info
 File 35:Dissertation Abs Online 1861-2003/Jan
 (c) 2003 ProQuest Info&Learning
 File 50:CAB Abstracts 1971-2002/Dec
 (c) 2003 CAB International
 File 71:ELSEVIER BIOBASE 1934-2003/Feb W1
 (c) 2003 Elsevier Science B.V.
 File 73:EMBASE 1974-2003/Jan W4
 (c) 2003 Elsevier Science B.V.
 File 94:JICST-EPlus 1985-2003/Nov W3
 (c) 2003 Japan Science and Tech Corp(JST)
 File 144:Pascal 1973-2003/Jan W4
 (c) 2003 INIST/CNRS
 File 281:ONTAP(R) Gale Group MARS(R)
 (c) 1999 The Gale Group
 File 340:CLAIMS(F)/US Patent 1950-03/Jan 30
 (c) 2003 IFI/CLAIMS(R)
 File 345:Inpadoc/Fam. & Legal Stat 1968-2002/UD=200304
 (c) 2003 EPO
 File 351:Derwent WPI 1963-2003/UD,UM &UP=200307
 (c) 2003 Thomson Derwent
 File 357:Derwent Biotech Res. 1982-2003/Feb W1
 (c) 2003 Thomson Derwent & ISI
 File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
 (c) 1998 Inst for Sci Info
 File 440:Current Contents Search(R) 1990-2003/Feb 04
 (c) 2003 Inst for Sci Info

nds

| Set | Items | Description |
|-----|-------|---|
| S1 | 3 | HISTACALIN(5W)PROTEIN? AND (ECTOPARASITE? OR TICK?) AND (C- ONJUNCTIVIT? OR EYE? OR OCUL?) |
| S2 | 3 | FD (unique items) |

pt2/7/1-3

2/7/1 (Item 1 from file: 340)
 DIALOG(R)File 340:CLAIMS(R)/US Patent
 (c) 2003 IFI/CLAIMS(R). All rts. reserv.

10207792 2002-0151499 2002-0039229
 C/TREATMENT OF CONJUNCTIVITIS
 Document Type: Utility
 Document Type: Patent Application-First Publication
 Inventors: Nuttall Patricia Anne (GB); Paesen Guido Christiaan (GB)
 Assignee: Unassigned Or Assigned To Individual
 Assignee Code: 68000

| | Kind | Publication Number | Date | Application Number | Date |
|------------------|------|-----------------------|----------|-----------------------|----------|
| | A1 | US 20020151499 | 20021017 | US 200285572 | 20020227 |
| Continuation of: | | UNKNOWN | | WO 2000GB3282 | 20000824 |
| Priority Applic: | | | | GB 99206740 | 19990901 |

Abstract: The present invention relates to the discovery that various

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proteins isolated from ticks are effective in the treatment of conjunctivitis. These proteins may most suitably be applied topically to an affected area and are effective to ameliorate the symptoms of this condition.

Exemplary Claim: D R A W I N G

1. Use of a histacalin protein (as defined herein) in the manufacture of a medicament for the treatment or prevention of conjunctivitis.

2/7/2 (Item 1 from file: 351)
DIALOG(R) File 351:Derwent WPI
(c) 2003 Thomson Derwent. All rts. reserv.

013773464

WPI Acc No: 2001-257675/200126

Use of histacalin proteins for treating or preventing non-infective conjunctivitis, or for manufacturing a medicament for treating or preventing conjunctivitis, e.g. seasonal or perennial allergic conjunctivitis

Patent Assignee: EVOLUTEC LTD (EVOL-N); NUTTALL P A (NUTT-I); PAESEN G C (PAES-I)

Inventor: NUTTALL P A; PAESEN G C

Number of Countries: 095 Number of Patents: 005

Patent Family:

| Patent No | Kind | Date | Applicat No | Kind | Date | Week |
|----------------|------|----------|---------------|------|----------|----------|
| WO 200115719 | A2 | 20010308 | WO 2000GB3282 | A | 20000824 | 200126 B |
| AU 200067139 | A | 20010326 | AU 200067139 | A | 20000824 | 200137 |
| BR 200013665 | A | 20020514 | BR 200013665 | A | 20000824 | 200240 |
| | | | WO 2000GB3282 | A | 20000824 | |
| EP 1207893 | A2 | 20020529 | EP 2000954784 | A | 20000824 | 200243 |
| | | | WO 2000GB3282 | A | 20000824 | |
| US 20020151499 | A1 | 20021017 | WO 2000GB3282 | A | 20000824 | 200270 |
| | | | US 200285572 | A | 20020227 | |

Priority Applications (No Type Date): GB 9920674 A 19990901

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 200115719 A2 E 19 A61K-038/00

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GR GM HE HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GR IE IT IE IT KE LS LU MC MW NZ NL OA PT SD SE SL SZ TZ UG ZW

AU 200067139 A A61K-038/00 Based on patent WO 200115719

BR 200013665 A A61K-038/00 Based on patent WO 200115719

EP 1207893 A2 E A61K-038/17 Based on patent WO 200115719

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

US 20020151499 A1 A61K-038/17 Cont of application WO 2000GB3282

Abstract (Basic): WO 200115719 A2

NOVELTY - Employing a histacalin protein for treating or preventing conjunctivitis, or for manufacturing a medicament for treating or preventing conjunctivitis.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) use of a histacalin protein in the manufacture of a medicament for treating or preventing conjunctivitis;

(2) a pharmaceutical composition comprising a histacalin protein, an antihistamine and a pharmaceutical carrier; and

(3) a method for treating or preventing conjunctivitis comprising administering to a subject a dose of the histacalin protein or the pharmaceutical composition.

ACTIVITY - Anti-inflammatory; antiallergic; antihistamine; ophthalmological.

MECHANISM OF ACTION - Histamine inhibitor.

USE - The histacalin protein, pharmaceutical composition or method is useful for treating or preventing conjunctivitis, which is non-infective. Preferably, these are useful for treating or preventing allergic conjunctivitis, e.g. seasonal or perennial allergic conjunctivitis (all claimed). These are also useful in treating or preventing vernal keratoconjunctivitis, giant papillary conjunctivitis or atopic keratoconjunctivitis. The histacalin protein may also be used as a diagnostic tool for evaluating the disease state of a patient suffering from non-infective conjunctivitis. Histacalin protein FS-HBP2 (designated EV131) ophthalmic solution was prepared in 1 % and 6 % concentrations from stock that contained approximately 2 mg EV131 and 50 microl dH2O. Treatment was with either saline, or with 1 % or 6 % EV131 using the rabbit model. Each rabbit was topically dosed in the right eye with 40 microl EV131, and the left eye with 40 microl saline. Five rabbits were dosed with 1 % EV131 and four rabbits were dosed with 6 % EV131. Ten minutes following dosing, 25 microl of 7.5 mg/ml of a solution of Compound 48/80 (a pro-inflammatory compound that promotes the release of allergy mediators, including histamine). A dose of 6 % EV131 was found to give optimum results of consistent reduction in inflammation as measured by hyperemia, chemosis, mucus discharge or lid swelling.

pp: 19 DwgNo. 0/6

Derwent Class: B04

International Patent Class (Main): A61K-038/00; A61K-038/17

International Patent Class (Additional): A61P-037/08

2/7/3 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI
(c) 2003 Thomson Derwent. All rts. reserv.

013734291

WPI Acc No: 2001-218521/200122

Use of histacalin proteins for treating or preventing allergic rhinitis, or for manufacturing a medicament for treating or preventing allergic rhinitis, e.g. seasonal or perennial allergic rhinitis
Patent Assignee: EVOLUTEC LTD (EVOL-N); NUTTALL P A (NUTT-I); PAESEN G C (PAES-I)

Inventor: NUTTALL P A; PAESEN G C

Number of Countries: 095 Number of Patents: 006

Patent Family:

| Patent No | Kind | Date | Applicat No | Kind | Date | Week |
|----------------|------|----------|---------------|------|----------|----------|
| WO 200116164 | A2 | 20010308 | WO 2000GB3287 | A | 20000824 | 200122 B |
| AU 200067143 | A | 20010326 | AU 200067143 | A | 20000824 | 200137 |
| BR 200013655 | A | 20020507 | BR 200013655 | A | 20000824 | 200238 |
| | | | WO 2000GB3287 | A | 20000824 | |
| EP 1207899 | A2 | 20020529 | EP 2000954788 | A | 20000824 | 200243 |
| | | | WO 2000GB3287 | A | 20000824 | |
| US 20020193306 | A1 | 20021219 | WO 2000GB3287 | A | 20000824 | 200303 |
| | | | US 200287195 | A | 20020301 | |
| CN 1374471 | A | 20021002 | CN 2000812372 | A | 20000824 | 200307 |

Priority Applications (No Type Date): GB 9920673 A 19990901

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 200116164 A2 E 19 C07K-014/00

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA
CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU IL IN IS JP
KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT
PO PU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR
IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

AU 200067143 A C07K-014/00 Based on patent WO 200116164

BR 200013655 A C07K-014/00 Based on patent WO 200116164

EP 1207899 A2 E A61K-038/17 Based on patent WO 200116164

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT
LI LT LU LV MC MK NL PT RO SE SI

US 20010193306 A1 A61K-038/17 Cont of application WO 2000GB3287

CN 1372471 A A61K-038/17

Abstract (Basic): WO 200116164 A2

NOVELTY - Employing a histacalin protein for treating or preventing allergic rhinitis, or for manufacturing a medicament for treating or preventing allergic rhinitis.

ACTIVITY - Antiinflammatory; antiallergic; ophthalmological.

Three subjects were challenged intranasally with histamine at 0.5, 1.0, 2.0, 4.0 or 8 mg/ml concentrations. 45 minutes after the completion of the challenge, baseline measurements were taken. Then a histacalin protein MS-HBP1 (designated EV504) was administered as a fresh solution of pre-weighed aliquots of histacalin in phosphate buffered saline. The solution was administered by dropping from a pipette into each nostril. After a further 15 minutes, a repeat nasal histamine dose-response challenge was administered. The results were recorded as total nasal airway resistance, as measured by active posterior rhinomanometry, and by measurement of anterior nasal secretions. Results showed that anterior nasal secretions and nasal airway resistance was greatly reduced upon administration of the histacalin protein.

MECHANISM OF ACTION - Histamine inhibitor.

USE - The histacalin protein, the medicament or method is useful for treating or preventing allergic rhinitis, both seasonal and perennial allergic conjunctivitis (claimed).

pp; 19 DwgNo 9/8

Derwent Class: B04

International Patent Class (Main): A61K-038/17; C07K-014/00

International Patent Class (Additional): A61P-037/C8

?ds

| Set | Items | Description |
|-----|-------|---|
| S1 | 3 | HISTACALIN(5W)PROTEIN? AND (ECTOPARASITE? OF TICK?) AND (C-ONJUNCTIVIT? OR EYE? OR OCUL?) |
| S2 | 3 | FD (unique items) |
| S3 | 3600 | MS(W) (HBP1 OR HBP(W)1) OR FS(W) (HBP1 OR HBP(W)1) OR FS(W) (-HBP2 OR HBP(W)1) OR D(W)RET6 OR D(W)RET(W)6 OR D(W)RET? |
| S4 | 2723 | FD (unique items) |
| S5 | 49 | S4 AND (CONJUNCTIV? OR EYE? OR OCUL?) |
| S6 | 2720 | S4 NOT S2 |
| S7 | 28 | S6(S) (CONJUNCTIV? OF EYE? OR OCUL?) |
| S8 | 6 | S3 NOT D(W)RET? |
| S9 | 3 | S8 NOT S2 |

?t9/1-3

9/7/1 (Item 1 from file: 340)

DIALOG(F)File 340:CLAIMS(R)/US Patent

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10249599 2002-0193306 2002-0050215

C/TREATMENT OF ALLERGIC RHINITIS

Document Type: Utility

Document Type: Patent Application-First Publication

**

00001000

Inventors: Nuttall Patricia Anne (GB); Paesen Guido Christiaan (GB)

Assignee: Unassigned Or Assigned To Individual

Assignee Code: 68000

| | Kind | Publication Number | Date | Application Number | Date |
|------------------|------|-----------------------|----------|-----------------------|----------|
| | A1 | US 20020193306 | 20021219 | US 200287195 | 20020301 |
| Continuation of: | | UNKNOWN | | WO 2000GB3287 | 20000824 |
| Priority Applic: | | | | GB 99206732 | 19990901 |

Abstract: The invention relates to the discovery that various proteins isolated from ticks are effective in the treatment and prevention of allergic rhinitis. These proteins may most suitably be applied to an affected area and are thus effective to treat this condition and to ameliorate its symptoms.

Exemplary Claim:

D R A W I N G

1. Use of a histacalin protein (as defined above) in the manufacture of a medicament for the treatment or prevention of allergic rhinitis.

9/7/2 (Item 1 from file: 351)
 DIALOG(R)File 351:Derwent WPI
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012551734

WPI Acc No: 1999-357841/199930

Histamine and serotonin binding compounds useful for the treatment of allergies

Patent Assignee: OXFORD VACS LTD (OXFO-N)

Inventor: NUTTALL P A; PAESEN G C

Number of Countries: 084 Number of Patents: 010

Patent Family:

| Patent No | Kind | Date | Applicat No | Kind | Date | Week |
|---------------|------|----------|---------------|------|----------|----------|
| WO 9927104 | A1 | 19990603 | WO 98GB3530 | A | 19981126 | 199930 B |
| AU 9912511 | A | 19990615 | AU 9912511 | A | 19981126 | 199944 |
| EP 1034273 | A1 | 20000913 | EP 98955786 | A | 19981126 | 200046 |
| | | | WO 98GB3530 | A | 19981126 | |
| BF 9815056 | A | 20001003 | BF 9815056 | A | 19981126 | 200053 |
| | | | WO 98GB3530 | A | 19981126 | |
| CZ 200001927 | A3 | 20001011 | WO 98GB3530 | A | 19981126 | 200060 |
| | | | CZ 20001917 | A | 19981126 | |
| SK 200000791 | A3 | 20001211 | WO 98GB3530 | A | 19981126 | 200103 |
| | | | SK 2000791 | A | 19981126 | |
| CN 1286726 | A | 20010307 | CN 98813321 | A | 19981126 | 200140 |
| MX 2000005010 | A1 | 20010501 | MX 20005010 | A | 20000522 | 200227 |
| JP 2002508927 | W | 20020326 | WO 98GB3530 | A | 19981126 | 200236 |
| | | | JP 2000522246 | A | 19981126 | |
| NZ 504753 | A | 20021122 | NZ 504753 | A | 19981126 | 200301 |
| | | | WO 98GB3530 | A | 19981126 | |

Priority Applications (No Type Date): GB 9813917 A 19980626; GB 9725046 A 19971126

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 9927104 A1 E 84 C12N-015/21

Designated States (National): AL AM AT AU AZ BA BB BG BF BY CA CH CN CU
DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TR
TM TR TT UA UG US UZ VN YU ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR
IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9912511 A C12N-015/21 Based on patent WO 9917104

EP 1034273 A1 E C12N-015/21 Based on patent WO 9917104

Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI
LU MC NL PT RO SE

BR 9815056 A C12N-015/21 Based on patent WO 9917104

CZ 200001927 A3 C12N-015/21 Based on patent WO 9917104

SK 200000791 A3 C12N-015/21

CN 1286726 A C12N-015/21

MX 2000005010 A1 A01K-057/027

JP 2002503927 W 95 C12N-015/09 Based on patent WO 9917104

NZ 504753 A C12N-015/21 Based on patent WO 9917104

Abstract (Basic): WO 9927104 A1

NOVELTY - Histamine or serotonin binding compounds (A), are new.

DETAILED DESCRIPTION - (A) has a dissociation constant of less than 10⁻⁷ M and a binding site that includes:

(a) Phe, Ile, or Leu at residue I, Trp at residue II, and Asp or Glu at III and IV where residues I-IV are positioned as in residues 103, 42, 39, and 82 of sequences (I) (190 aa, given in the specification) or (II) (190 aa, given in the specification), residues 107, 41, 38, and 78 of sequence (III) (200 aa given in the specification), or residues 122, 54, 50, and 95 of sequence (IV) (209 aa given in the specification).

INDEPENDENT CLAIMS are also included for the following:

(1) compounds as above with Phe or Ile at residue I, Trp at residue II, and Asp or Glu at residue III or IV of the binding site where residues I-IV are positioned according to residues 98, 137, 24, and 120 of sequences (I) or (II), residues 95, 138, 23, and 120 of sequence (III), or residues 112, 149, 35, and 135 of sequence (IV);

(2) a histamine binding compound capable of binding histamine or serotonin that has 2 binding sites, 1 as in (a), the other as in (1);

(3) a protein comprising Ra-Res of amino acid sequence (V) (207 aa, given in the specification), or an equivalent derivative or fragment;

(4) a protein comprising Av-HBP of amino acid sequence (VI) (178 aa, given in the specification), or an equivalent derivative or fragment;

(5) a protein comprising Ih/Bm-HBP1 of amino acid sequence (VII) (203 aa, given in the specification), or an equivalent derivative or fragment;

(6) a protein comprising Ih/Bm-HBP2 of amino acid sequence (VIII) (203 aa, given in the specification), or an equivalent derivative or fragment;

(7) a protein comprising Ih/Bm-HBP3 of amino acid sequence (IX) (285 aa, given in the specification), or an equivalent derivative or fragment;

(8) a protein comprising Ih/Bm-HBP4 of amino acid sequence (X) (284 aa, given in the specification), or an equivalent derivative or fragment;

(9) a protein comprising Ih/Bm-HBP5 of amino acid sequence (XI) (321 aa, given in the specification), or an equivalent derivative or fragment.

(10) a nucleic acid encoding a compound of claims (a) and (1)-(9);

(11) a vector containing the nucleic acid molecule of (10);

(12) a host cell transformed with the vector of (11); and

(13) a transgenic animal transformed by the nucleic acid of (11) or

the vector of (12).

ACTIVITY - Anti-inflammatory; antihistamine; antiallergic; anti-asthmatic; cytostatic; antimigrane; dermatological;

MECHANISM OF ACTION - Histamine and serotonin binding.

USE - The compounds are useful for regulating the action of histamine and serotonin (in e.g. inflammation and gastric acid secretion), the detection, quantification and removal of histamine or serotonin (in animals, plants, cell cultures, food materials, or humans) and in the treatment of various diseases and allergies (e.g. type I hypersensitivity reactions, urticaria, asthma, allergic rhinitis (hay fever), atopic dermatitis, insect bites and food and drug allergies, abnormal blood pressure, migraine, psychological disorders, respiratory disease, and coronary heart disease). Histamine may also be used to regulate cellular growth and tissue repair. The molecules may also be used as components of vaccines directed against blood-sucking ectoparasites.

pp; 84 DwgNo 0/22

Derwent Class: B04; C03; C06; D13; D16; P14; S03

International Patent Class (Main): A01K-057/027; C12N-015/09; C12N-015/21

International Patent Class (Additional): A01K-067/027; A23L-001/015;

A23L-001/05; A61K-031/19; A61K-031/35; A61K-031/40; A61K-031/66;

A61K-038/00; A61K-038/17; A61K-045/00; A61K-048/00; A61P-037/00;

A61P-043/00; C07K-014/435; C07K-017/00; C12N-001/21; C12N-005/10;

C12N-015/00; G01N-033/68

9/7/3 (Item 2 from file: 351)
DIALOG(R) File 351: Derwent WPI
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011601378

WPI Acc No: 1998-018506/199802

New vasoactive amine binding proteins and related nucleic acid, vectors - transformed cells and transgenic animals, used for assaying or removing histamine and as antihistamine or anti-inflammatory agents

Patent Assignee: OXFORD VACS LTD (OXFO-N)

Inventor: NUTTALL P A; PAESEN G C

Number of Countries: 077 Number of Patents: 009

Patent Family:

| Patent No | Kind | Date | Applicat No | Kind | Date | Week |
|---------------|------|----------|-------------|------|----------|----------|
| WO 9744451 | A2 | 19971127 | WO 97GB1372 | A | 19970519 | 199802 B |
| AU 9729071 | A | 19971209 | AU 9729071 | A | 19970519 | 199824 |
| EP 906425 | A2 | 19990407 | EP 97923204 | A | 19970519 | 199916 |
| | | | WO 97GB1372 | A | 19970519 | |
| CN 1235683 | A | 19990811 | CN 97196317 | A | 19970519 | 199950 |
| BR 9709101 | A | 19990803 | BR 979101 | A | 19970519 | 199952 |
| | | | WO 97GB1372 | A | 19970519 | |
| NZ 332648 | A | 20000526 | NZ 332648 | A | 19970519 | 200033 |
| | | | WO 97GB1372 | A | 19970519 | |
| JP 1000512489 | W | 20000926 | JP 97541799 | A | 19970519 | 200051 |
| | | | WO 97GB1372 | A | 19970519 | |
| MX 9809509 | A1 | 19990301 | MX 989509 | A | 19981113 | 200051 |
| AU 725630 | B | 20001019 | AU 9729071 | A | 19970519 | 200057 |

Priority Applications (No Type Date): GB 977844 A 19970418; GB 9610484 A 19960518

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 9744451 A2 E 44 C12N-C15/12

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG

US US VN YU

Designated States (Regional): AT BE CH DE DK EA ES FI FR GB GH GR IE IT
KE LS LU MC MW NL OA PT SD SE SZ UG

AU 9729071 A C12N-015/12 Based on patent WO 9744451

EP 906425 A2 E C12N-015/12 Based on patent WO 9744451

Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LI LU
MC NL PT RO SE

CN 1225683 A C12N-015/12

BR 9709101 A C12N-015/12 Based on patent WO 9744451

NZ 332648 A C12Q-001/68 Based on patent WO 9744451

JP 2000512489 W 44 C12N-015/09 Based on patent WO 9744451

MX 9809509 A1 C12N-015/12

AU 725630 B C12N-015/12 Previous Publ. patent AU 9729071

Based on patent WO 9744451

Abstract (Basic): WO 9744451 A

Vasoactive amine binding proteins (VABP) that bind specifically to vasoactive amines (VA) with dissociation constant below 0.1 μ M and belong to the same protein family as MS - HBPI ; FS - HBPI or 2, or D . RET6 are new. Also new are (1) functional fragments and derivatives of VABP; (2) nucleic acid (I) encoding VABP or hybridising with the coding sequence; (3) cloning or expression vectors containing (I); (4) host cells transformed or transfected with these vectors; (5) transgenic animals containing (I).

USE - The host cells are used to produce recombinant VABP. VABP are used (i) to detect or quantify histamine (or other VA such as serotonin) in body fluids or cell culture supernatants, e.g. to monitor the effect of allergens; (ii) for binding VA, e.g. to remove histamine from blood, food, cell cultures etc.; (iii) as an antihistamine or anti-inflammatory agent, e.g. for treating insect, snake or scorpion bites or dermatitis, or as a carrier for slow release of histamine-related compounds; (iv) in vaccines to protect against metazoan parasites, especially in animals; (v) as reagents for studying inflammation, involvement of VA in ulcer formation or the immune response etc.

ADVANTAGE - VABP provide a more sensitive assay for histamine than low-affinity antibodies currently used. They may also be more effective and safer than conventional antihistamines.

Dwg.0/10

Derwent Class: B04; D16; P14; S03

International Patent Class (Main): C12N-015/09; C12N-015/12; C12Q-001/68

International Patent Class (Additional): A01K-067/027; A61K-035/56;

A61K-035/58; A61K-035/64; A61K-038/17; A61K-039/38; C07K-014/435;

C07K-017/00; C07K-019/00; C12N-005/10; C12N-015/62; C12N-015/86;

C12P-021/02; G01N-033/68

?